

### **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application.

### **Listing of Claims:**

1 – 113. (Cancelled)

114. (Previously presented) An isolated protein that is free of all central nervous system myelin material comprising an amino acid sequence selected from the group consisting of

the polypeptide of SEQ ID NO: 2, and

amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2.

115. (Previously presented) An isolated protein that is free of all central nervous system myelin material comprising an amino acid sequence selected from the group consisting of

an amino acid sequence in which more than 90% of the amino acid residues in said sequence are identical to the amino acid residues of SEQ ID NO:2 in an alignment, and

an amino acid sequence in which more than 90% of the amino acid residues in said sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2,

wherein said protein has one or more Nogo functional activities selected from the group consisting of: (i) ability to bind to an antibody to a protein consisting of SEQ ID NO:2 or consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2; (ii) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:2 or consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2; (iii) ability to prevent regeneration of neurons in the spinal cord or brain; (iv) ability to confer to a substrate the property of restricting growth, spreading, and migration of neural cells; (v)

ability to inhibit dorsal root ganglia neurite outgrowth; (vi) ability to block NIH 3T3 cell spreading *in vitro*; and (vii) ability to block PC12 neurite outgrowth.

116. (Previously presented) An isolated protein that is free of all central nervous system myelin material comprising an amino acid sequence selected from the group consisting of

an amino sequence in which more than 95% of the amino acid residues in said sequence are identical to the amino acid residues of SEQ ID NO:2 in an alignment, and

an amino acid sequence in which more than 95% of the amino acid residues in said sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2,

wherein said protein has one or more Nogo functional activities selected from the group consisting of: (i) ability to bind to an antibody to a protein consisting of SEQ ID NO:2 or consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2; (ii) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:2 or consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2; (iii) ability to prevent regeneration of neurons in the spinal cord or brain; (iv) ability to confer to a substrate the property of restricting growth, spreading, and migration of neural cells; (v) ability to inhibit dorsal root ganglia neurite outgrowth; (vi) ability to block NIH 3T3 cell spreading *in vitro*; and (vii) ability to block PC12 neurite outgrowth.

117. (Previously presented) An isolated protein that is free of all central nervous system myelin material comprising an amino acid sequence selected from the group consisting of

the polypeptide of SEQ ID NO: 29, and

amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO: 29.

118. (Previously presented) An isolated protein that is free of all central nervous system myelin material comprising

an amino sequence in which more than 90% of the amino acid residues in said sequence are identical to the amino acid residues of SEQ ID NO:29 in an alignment

wherein said protein has one or more Nogo functional activities ~~activity~~ selected from the group consisting of: (i) ability to bind to an antibody to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; (ii) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; (iii) ability to prevent regeneration of neurons in the spinal cord or brain; (iv) ability to confer to a substrate the property of restricting growth, spreading, and migration of neural cells; (v) ability to inhibit dorsal root ganglia neurite outgrowth; (vi) ability to block NIH 3T3 cell spreading *in vitro*; and (vii) ability to block PC12 neurite outgrowth.

119. (Previously presented) An isolated protein that is free of all central nervous system myelin material comprising

an amino sequence in which more than 95% of the amino acid residues in said sequence are identical to the amino acid residues of SEQ ID NO:29 in an alignment

wherein said protein has one or more Nogo functional activities selected from the group consisting of: (i) ability to bind to an antibody to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; (ii) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; (iii) ability to prevent regeneration of neurons in the spinal cord or brain; (iv) ability to confer to a substrate the property of restricting growth, spreading, and migration of neural cells; (v) ability to inhibit dorsal root ganglia neurite outgrowth; (vi) ability to block NIH 3T3 cell spreading *in vitro*; and (vii) ability to block PC12 neurite outgrowth.

120. to 122. (Cancelled)

123. (Previously presented) The protein of any one of claims 115, 116, 118, or 119, wherein said protein is mammalian.

124. (Previously presented) The protein of any one of claims 118, or 119, wherein said protein is human.

125. (Previously presented) The protein of any one of claims 114, 115, 116, 117, 118, or 119, wherein said protein is recombinant.

126. (Previously presented) An isolated nucleic acid comprising a polynucleotide which encodes a protein comprising an amino acid sequence selected from the group consisting of

the polypeptide of SEQ ID NO: 2,

amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2,

the polypeptide of SEQ ID NO: 29, and

amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO: 29.

127. (Previously presented) An isolated nucleic acid comprising a polynucleotide which hybridizes to a second nucleic acid which consists of a nucleotide coding sequence which encodes the amino acid sequence of SEQ ID NO: 2, amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2, SEQ ID NO: 29, or amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO: 29, under high stringency conditions comprising:

(a) hybridization in 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% of a copolymer of sucrose and epichlorohydrin 0.02% BSA, and 100 µg/ml denatured salmon sperm DNA at 65°C; and

(b) washing in a solution containing 2X SSC, 0.01% PVP, 0.01% of a copolymer of sucrose and epichlorohydrin, and 0.01% BSA at 37°C for 1 h, and subsequently in 0.1X SSC at 50°C for 45 min;

wherein the polynucleotide encodes a protein that displays inhibitory activity in an NIH 3T3 fibroblast spreading assay.

128. (Previously presented) An expression vector comprising a nucleotide sequence which encodes a protein comprising an amino acid sequence selected from the group consisting of

the polypeptide of SEQ ID NO: 2,

amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2,

the polypeptide of SEQ ID NO: 29, and

amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO: 29.

129. (Previously presented) An *ex vivo* recombinant host cell comprising the expression vector of claim 128.

130. (Previously presented) The *ex vivo* recombinant host cell of claim 129 wherein the recombinant host cell is a prokaryotic cell.

131. (Previously presented) The *ex vivo* recombinant host cell of claim 129 wherein the recombinant host cell is a eukaryotic cell.

132. (Previously presented) A method of producing a recombinant protein comprising culturing a recombinant host cell transformed with the nucleic acid of claim 126 such that the protein encoded by said nucleic acid is expressed by said cell and recovering said expressed protein.

133- 134 (Canceled)

135. (Currently amended) An isolated protein, wherein the protein (a) is free of all central nervous system myelin material; ~~and~~ (b) has one or more Nogo functional activities selected from the group consisting of: (i) ability to bind to an antibody to a protein consisting of SEQ ID NO:2 or consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2; (ii) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:2 or consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2; (iii) ability to bind to an antibody to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; and (iv) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; and (c) comprises

- (i) an amino acid sequence consisting of amino acids 623 to 640 of SEQ ID NO:2;
- (ii) an amino acid sequence consisting of the amino acid sequence of SEQ ID NO:43;
- (iii) an amino acid sequence consisting of the amino acid sequence of SEQ ID NO:44;
- (iv) an amino acid sequence consisting of the amino acid sequence of SEQ ID NO:45;
- (v) an amino acid sequence consisting of the amino acid sequence of SEQ ID NO:46;

or

- (vi) an amino acid sequence consisting of amino acids 762-1163 of SEQ ID NO:2.

136. (Currently amended) An isolated protein, wherein the protein (a) is free of all central nervous system myelin material; ~~and~~ (b) has one or more Nogo functional activities selected from the group consisting of: (i) ability to bind to an antibody to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; and (ii) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; and (c) consists of

- (i) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence

in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 1-131 of SEQ ID NO:29;

(ii) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 132-939 of SEQ ID NO:29;

(iii) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 206-501 of SEQ ID NO:29;

(iv) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 501-680 of SEQ ID NO:29;

(v) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 132-206 of SEQ ID NO:29;

(vi) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 680-939 of SEQ ID NO:29; or

(vii) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 940-1127 of SEQ ID NO:29.

137. (Previously presented) An isolated protein, wherein the protein (a) is free of all central nervous system myelin material; and (b) comprises

(i) an amino acid sequence consisting of amino acids 132-939 of SEQ ID NO:29;

(ii) an amino acid sequence consisting of amino acids 206-501 of SEQ ID NO:29;

- (iii) an amino acid sequence consisting of amino acids 501-680 of SEQ ID NO:29; or
- (iv) an amino acid sequence consisting of amino acids 132-206 of SEQ ID NO:29.

138. (Currently amended) An isolated nucleic acid comprising a polynucleotide which

(i) hybridizes to a second polynucleotide under high stringency conditions comprising:

(a) hybridization in 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% of a copolymer of sucrose and epichlorohydrin, 0.02% BSA, and 100 µg/ml denatured salmon sperm DNA at 65°C; and

(b) washing in a solution containing 2X SSC, 0.01% PVP, 0.01% of a copolymer of sucrose and epichlorohydrin, and 0.01% BSA at 37°C for 1 h, and subsequently in 0.1X SSC at 50°C for 45 min;

wherein the second polynucleotide consists of a nucleotide coding sequence which encodes the amino acid sequence of SEQ ID NO: 2, amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2, SEQ ID NO: 29, or amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO: 29; and

(ii) encodes a protein, wherein the protein has one or more Nogo functional activities selected from the group consisting of: (i) ability to bind to an antibody to a protein consisting of SEQ ID NO:2 or consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2; (ii) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:2 or consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2; (iii) ability to bind to an antibody to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; and (iv) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29 ~~an antibody that binds to the protein also binds to a protein consisting of the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:29.~~



139. (Previously presented) An isolated protein, wherein the protein (a) is free of all central nervous system myelin material; and (b) comprises:

- (i) an amino acid sequence consisting of amino acids 31-57 of SEQ ID NO:2; or
- (ii) an amino acid sequence consisting of amino acids 1090-1125 depicted in Figure 2a (SEQ ID NO:2).

140. (Previously presented) An isolated protein, wherein the protein (a) is free of all central nervous system myelin material; and (b) consists of:

- (i) the carboxy-terminal 188 amino acids of SEQ ID NO:29;
- (ii) an amino acid sequence consisting of amino acids 988-1023 of SEQ ID NO:2;
- (iii) an amino acid sequence consisting of amino acids 975-1162 of SEQ ID NO:2;
- (iv) an amino acid sequence consisting of amino acids 172 to 974 of SEQ ID NO:2;
- (v) an amino acid sequence consisting of amino acids 172 to 723 of SEQ ID NO:2;
- (vi) an amino acid sequence consisting of amino acids 542 to 722 of SEQ ID NO:2;
- (vii) an amino acid sequence consisting of amino acids 1-171 of SEQ ID NO:2;
- (viii) an amino acid sequence consisting of amino acids 1-974 of SEQ ID NO:2;
- (ix) an amino acid sequence consisting of amino acids 1-131 of SEQ ID NO:29;
- (x) an amino acid sequence consisting of amino acids 680-939 of SEQ ID NO:29;
- (xi) an amino acid sequence consisting of amino acids 940-1127 of SEQ ID NO:29;
- (xii) an amino acid sequence consisting of amino acids 259-542 of SEQ ID NO:2;
- (xiii) an amino acid sequence consisting of amino acids 172-259 of SEQ ID NO:2; or
- (xiv) an amino acid sequence consisting of amino acids 722-974 of SEQ ID NO:2.

141. (Previously presented) The protein of any one of claims 135, 136, and 137, wherein the protein is non-naturally occurring.

142. (New) An isolated nucleic acid comprising a polynucleotide which encodes the protein of any one of claims 135 to 137, 139, and 140.

143. (New) A method of producing a recombinant protein comprising culturing a recombinant host cell transformed with the nucleic acid of claim 142 such that the protein encoded by said nucleic acid is expressed by said cell, and recovering said expressed protein.

144. (New) The method of claim 143, wherein the recovering step comprises purifying via a binding tag.

145. (New) A purified protein produced according to the method of claim 143, which method further comprises purifying said expressed protein, which purified protein is free of all central nervous system myelin material.

146. (New) A purified protein produced according to the method of claim 144, which method further comprises purifying said expressed protein, which purified protein is free of all central nervous system myelin material.